REMARKS

Claims 1, 9 to 13, 16, 17, 23, 26 to 30, 37, 38, 41 to 44, 46 to 48, 53, 57 to 60, 62 to 66, 81, 90, and 91 are currently pending in the instant application. Claims 2 to 8, 14, 15, 18 to 22, 24, 25, 31 to 36, 39, 40, 45, 49 to 52, 54 to 56, 61, 67, to 80, and 82 to 89 have been cancelled without prejudice or disclaimer.

Claim 1 has been amended to recite in pertinent part that "linker –B–C– is an optionally substituted linker of the formula $–CH_2(CH_2)_z–$, where z is 1;" "R_1 is optionally substituted aryl;" "R_2 is $–C(O)R_3$, where R_3 is selected from $–(CH_2)_m$ aryl and $–(CH_2)_m$ heterocyclyl, where m is 0 or 1;" and "X is O." Support for the amendments can be found, *e.g.*, on page 12, lines 4 to 18; page 13, lines 9 to 35; page 14, lines 8 to 11; and page 15, lines 1 to 6; and in original claims 15, 21, 24, and 25 of the corresponding PCT publication (WO 2005/061513, "the '513 publication").

Claim 13 has been amended to recite in pertinent part that "R_2 is $–C(O)R_3$." Support for the amendment can be found, *e.g.*, on page 14, lines 8 to 11, and original claim 15 of the '513 publication.

Claim 26 has been amended to recite in pertinent part that "R_1 represents phenyl." Support for the amendment can be found, *e.g.*, on page 13, lines 20 to 35 of the '513 publication.

Claim 28 has been amended to recite in pertinent part that "R_1 represents phenyl, substituted with halo, $C_{1\text{-}6}$ alkyl…." Support for the amendment can be found, *e.g.*, on page 13, lines 20 to 34 of the '513 publication.

Claim 38 has been amended to recite in pertinent part that "linker –B–C– is an optionally substituted linker of the formula $–CH_2(CH_2)_z–$, where z is 1;" "R_1 is optionally substituted aryl;" "R_2 is $–C(O)R_3$, where R_3 is selected from $–(CH_2)_m$ aryl and $–(CH_2)_m$ heterocyclyl, where m is 0 or 1;" and "X is O." Support for the amendments can be found, *e.g.*, on page 12, lines 4 to 18; page 13, lines 9 to 35; page 14, lines 8 to 11; and page 15, lines 1 to 6; and in original claims 15, 21, 24, and 25 of the '513 publication.

Claim 44 has been amended to recite in pertinent part that "R_2 is $–C(O)R_3$." Support for the amendment can be found, *e.g.*, on page 14, lines 8 to 11, and original claim 15 of the '513 publication.

Claim 57 has been amended to recite in pertinent part that "R_1 represents phenyl." Support for the amendment can be found, *e.g.*, on page 13, lines 20 to 35 of the '513 publication.

Claims 62 and 64 have each been amended to recite in pertinent part that "R_2 is $-C(O)R_3$, where R_3 is selected from $-(CH_2)_m$ aryl and $-(CH_2)_m$ heteroaryl." Support for the amendments can be found, *e.g.*, page 14, lines 8 to 11 of the '513 publication.

Claim 65 has been amended to recite in pertinent part that "A compound selected from…and salts or pharmaceutically acceptable derivatives thereof." Support for the amendments can be found, *e.g.*, on page 15, line 21 to page 16, line 16 of the '513 publication.

Claims 90 and 91 are new. Support for the claims can be found, *e.g.*, on page 14, lines 16 to 27 of the '513 publication.

Applicants reserve the right to pursue the subject matter of unclaimed subject matter in the instant application in one or more divisional, continuation, and/or continuation in part applications. Applicants submit that the instant claims are fully supported by the specification as filed originally, and no new matter has been introduced.

A. <u>The Rejection under 35 U.S.C. § 112, First Paragraph, against Claims 1, 2, 9 to 31, and 35 to 37 Should Be Withdrawn</u>

In the Office Action, claims 1, 2, 9 to 31, and 35 to 37 stand rejected under 35 U.S.C. §112, first paragraph, allegedly for lack of enablement for some compounds of Formula I. Applicants respectfully disagree.

In the December 8, 2011 Final Action, the Examiner once more acknowledges that the instant claims are enabled for "treating the viral infection with compound [sic] defined by formula I, wherein A is <u>pyridyl</u> [sic], R1 is <u>a phenyl or substituted phenyl</u>, and R2 is <u>COR3</u> wherein R3 is <u>optionally substituted aryl</u>, X is <u>oxygen</u>." *See*, Item 8 on page 2 of the Final Action.

Solely to expedite prosecution, and without prejudice or disclaimers, instant claim 1 has been amended closely in line with this enablement acknowledged by the Examiner. In pertinent part, instant claim 1 recites that "A, together with the atoms to which it is attached, forms an

optionally substituted pyridyl ring;" "R_1 is optionally substituted aryl;" "R_2 is $-C(O)R_3$, where R_3 is selected from $-(CH_2)_m$ aryl and $-(CH_2)_m$ heterocyclyl; where m is 0 or 1;" and "X is O."

Applicants respectfully submit that instant claim 1 as amended is fully enabled by the instant specification as filed originally. For example, the limitation that R_3 is $-(CH_2)_m$ aryl and m is 1 in claim 1 is exemplified with compounds 351 and 371, which each have $-CH_2$-Ph as R_3 and have been found to be active against RSV. *See*, Table 7 on page 96 of the '513 publication. The limitation that R_3 is $-(CH_2)_m$ heterocyclyl and m is 0 in claim 1 is exemplified with compounds 363, 364, 366 to 370, 377, 379, 381, 382, 385 to 387, 391, 392, 394, 395, 397 to 399, 401, 404 to 406, 408, 409, 412 to 416, 420 to 423, 430, 431, 434, 436 to 438, 441, 442, 444, 445, 448 to 450, 453 to 458, 461 to 465, 467, 468, 474, and 480 to 484, which each have a 5-membered heterocyclyl (*e.g.*, furyl, thienyl, isoxazolyl, oxazolyl, pyrazolyl, isothiazolyl, thiazolyl, oxadiazolyl, triazolyl, or thiadiazolyl), 6-membered heterocyclyl (*e.g.*, pyridyl or pyrimidyl), or bicyclic heterocyclyl (*e.g.*, benzothiophenyl) as R_3 and have been found to be active against RSV. *See*, Table 7 on pages 96 and 97 of the '513 publication.

The Office Action further alleges that "Compounds 351 and 371 are the only two compounds with reported antiviral activity. The two compounds characterized with R2 as COR3 with R3 is –CH3-Aryl. The two compounds only show very weak antiviral activity (TABLE 7). One of ordinary skill in the art would have no reasonable expectation that such compounds would be useful for treating RSV viral infection." (Emphasis added). The Examiner insists on that this rejection is under 35 U.S.C. 112, first paragraph allegedly for lack of enablement, not under 35 U.S.C. 101 for lack of utility. *See*, page 2 of the March 17, 2011 Advisory Action. Even though this rejection is disguised under the enablement requirement of 35 U.S.C. 112, first paragraph, the language itself, in particular the word "USEFUL," used in the rejection, clearly indicates that this rejection is in fact based upon the utility requirement under either 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

However, "[[a]] 35 U.S.C. 112, first paragraph, rejection >based on lack of utility< should not be imposed or maintained unless an appropriate basis exists for imposing a >utility< rejection under 35 U.S.C. 101." "In other words, Office personnel should not impose a 35 U.S.C. 112, first paragraph, rejection grounded on a "lack of utility" basis unless a 35 U.S.C. 101 rejection is proper." "In particular, the factual showing needed to impose a rejection under 35

U.S.C. 101 must be provided if a rejection under 35 U.S.C. 112, first paragraph, is to be imposed on "lack of utility" grounds." (Emphasis added). MPEP 2107.01(IV).

As discussed previously, "[c]ourts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement." MPEP 2107.01(III) (citing *Nelson v. Bowler*, 626 F.2d 853, 856 (CCPA 1980)). "The Federal Circuit has reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs marketed in the United States." MPEP 2107.01(III) and MPEP 2164.06(a)(III) (Emphasis added). "Office personnel should not construe 35 U.S.C. 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans." MPEP 2107.01(III) and MPEP 2164.06(a)(III). Therefore, unless the Office Action can back up assertions of its own with acceptable evidence or reasoning as to why one of ordinary skill in the art would have no reasonable expectation that such compounds would be useful for treating RSV viral infections, "there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971).

Therefore, Applicants respectfully request that this rejection be withdrawn.

B. The Rejection under 35 U.S.C. § 103(a) against Claims 33, 38, 39, 41 to 60, 62 to 66, 81, and 86 Should Be Withdrawn

In the Office Action, claims 33, 38, 39, 41 to 60, 62 to 66, 81, and 86 stand rejected under 35 U.S.C. §103(a), allegedly as being unpatentable over Bamba *et al.* (WO 02/066479, "Bamba"). In particular, the Office Action alleges that "the compounds herein claimed encompass at least part of the compounds within the general formula disclosed in Bamba;" and "[t]therefore, one of ordinary skill in the art, need no more motivation other than following the instruction provided by Bamba to make the compounds herein claimed." Applicants respectfully disagree.

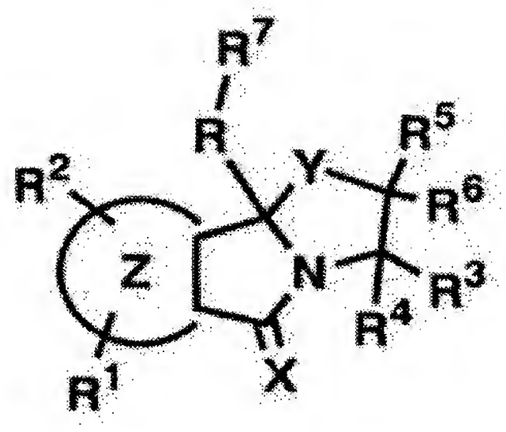
"The determination of obviousness is a matter of law based on findings of underlying fact, wherein the factors identified in *Graham v. John Deere Co.*, . . . guide the inquiry . . . ." *Sanofi-Synthelabo, Inc. v. Apotex, Inc.*, 550 F.3d 1075, 1085 (Fed. Cir. 2008), citing *Graham v.*

John Deere Co., 383 U.S. 1 (1966); *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 399 (2007). The factors identified in *Graham* are: (1) "the scope and content of the prior art;" (2) "the differences between the prior art and the claims;" (3) "the level of ordinary skill in the pertinent art;" and (4) "secondary considerations." *Graham*, 383 U.S. at 17–18. "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 401. It is important to identify "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.*

To establish a *prima facie* case of obviousness of new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner. *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). Furthermore, support for a proper *prima facie* case of obviousness of a new compound based on structural similarity of a prior art compound requires the identification of a reason as to why one of ordinary skill in the art would *select* and *modify* a known compound in a particular way to achieve the claimed compound. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008) (emphasis added). Even in light of *KSR*, the Federal Circuit has maintained that the chemical arts are often unpredictable, such that *KSR*'s focus on "identified predictable solutions" may present a difficult hurdle to overcome because potential solutions in the chemical arts are less likely to be genuinely predictable. *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996 (Fed. Cir. 2009). Thus, in order to establish a proper *prima facie* case of obviousness based on structural similarity, the Examiner must identify: (1) why one of ordinary skill in the art would have selected a particular compound from the cited reference as a lead compound; and (2) why one of ordinary skill in the art would have modified that particular compound in a particular way to arrive at the instantly claimed compounds. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008).

The Office Action fails to establish a *prima facie* case of obviousness for at least the reasons discussed herein.

First, the Office Action allegation that "the compounds herein claimed encompass at least part of the compounds within the general formula disclosed in Bamba" is inaccurate. For example, Bamba is directed to a compound having the structure of:



[I]

wherein Y can be NR^9. However, R^9, which corresponds to R^3 in the instant application, cannot be $-(CH_2)_m$ aryl or $-(CH_2)_m$ heteroaryl, which is required by the instant claims. *See*, page 16 of the English translation of the '479 publication. Therefore, there is no overlap between the instant claims and the general formula or specific compounds disclosed in Bamba.

Furthermore, Bamba fails to teach, suggest, or provide motivations to select $-(CH_2)_m$ aryl or $-(CH_2)_m$ heterocyclyl, specifically or generically, as R^9 to arrive at the instantly claimed compounds.

Additionally, the instant claims are directed toward compounds that are useful in treating RSV infections and methods for treating RSV infections. However, Bamba discloses compounds for treating diabetes. *See*, page 1 of the English translation of the '479 publication. Bamba is completely silent as to the treatment of RSV infections. The Office Action fails to articulate why one of ordinary skill in the art would have been motivated to select any possible compounds disclosed by Bamba, none of which had been shown to be active against RSV at the time of its disclosure, to arrive at the instantly claimed compounds that are active against RSV infections.

It is well established that the chemical arts are often unpredictable, and the modification of a lead compound often leads to different activity. *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996 (Fed. Cir. 2009). Thus, without the teaching of the instant application, one skilled in the art would have no reasonable expectation from the disclosure of Bamba that the instant compounds could be active against RSV and useful for treating RSV infections.

Therefore, the instant claims are not *prima facie* obvious, and reconsideration and withdrawal of the rejection are respectfully requested.

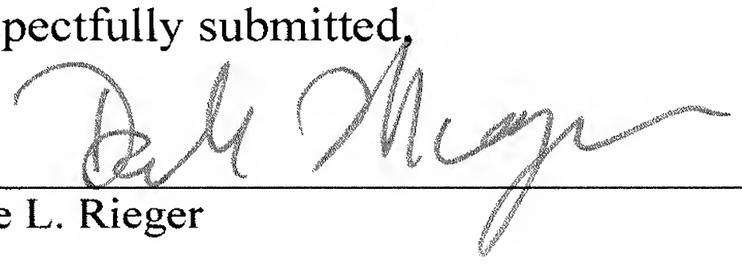
SUMMARY

Should the Examiner believe that prosecution of this application might be expedited by further discussion of any remaining issue, the Examiner is cordially invited to contact the undersigned representative of Applicants, Dale L. Rieger, Ph.D., by phone at (858) 314-1200 or by email at drieger@jonesday.com.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-3013 and please credit any excess fees to such deposit account.

Respectfully submitted,

Date: May 10, 2011



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